Complete Summary

GUIDELINE TITLE

Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus.

BIBLIOGRAPHIC SOURCE(S)

Sacks DB, Bruns DE, Goldstein DE, Maclaren NK, McDonald JM, Parrott M. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Clin Chem 2002 Mar;48(3):436-72. [267 references] PubMed

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Diabetes mellitus

GUIDELINE CATEGORY

Diagnosis
Management

CLINICAL SPECIALTY

Endocrinology
Family Practice
Internal Medicine
Nursing
Pathology

INTENDED USERS

Clinical Laboratory Personnel
Physicians

GUIDELINE OBJECTIVE(S)

- To provide recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus
- To supplement the American Diabetes Association (ADA) recommendations, with an emphasis on the laboratory aspects of diabetes

TARGET POPULATION

Patients with diabetes mellitus

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Screening

Plasma glucose measurement in an accredited laboratory

Management

1. Portable meters that measure plasma glucose concentrations for self-monitoring of blood glucose (SMBG)
2. Urine or blood ketone measurement
3. Glycated hemoglobin (GHb) performed in U.S. laboratories using assays certified by the National Glycohemoglobin Standardization Program (NGSP) as traceable to the Diabetes Control and Complications Trial (DCCT)
4. Microalbuminuria testing
5. Other laboratory studies, such as lipid profiles

Tests Considered but Not Recommended

- Portable meters, oral glucose tolerance test (OGTT), and noninvasive glucose analyses in the diagnosis of diabetes.
- Genetic markers for the diagnosis or management of diabetes
- Autoantibodies for routine diagnosis or screening of diabetes
- Routine testing for insulin, C-peptide, proinsulin, amylin, or leptin

MAJOR OUTCOMES CONSIDERED

Not stated

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The American Diabetes Association developed a system to grade the quality of scientific evidence in this guideline. This scheme has been used in this guideline to describe the quality of the evidence on which each recommendation is based.

A

Clear evidence from well-conducted, generalizable, randomized controlled trials that are adequately powered, including:

- Evidence from a well-conducted multicenter trial
- Evidence from a meta-analysis that incorporates quality ratings in the analysis
- Compelling nonexperimental evidence, i.e., "all or none" rule developed by the Center for Evidence Based Medicine at Oxford*

Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including:

- Evidence from a well-conducted trial at one or more institutions
- Evidence from a meta-analysis that incorporates quality ratings in the analysis

*Either all patients died before therapy and at least some survived with therapy, or some patients died without therapy and none died with therapy. Example: use of insulin in the treatment of diabetic ketoacidosis.

B

Supportive evidence from well-conducted cohort studies, including:

- Evidence from a well-conducted prospective cohort study or registry
- Evidence from a well-conducted metaanalysis of cohort studies

Supportive evidence from a well-conducted case-control study

C

Supportive evidence from poorly controlled or uncontrolled studies:

- Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results
- Evidence from observational studies with high potential for bias (such as case series with comparison to historical controls)
- Evidence from case series or case reports

Conflicting evidence with the weight of evidence supporting the recommendation

E

Expert consensus or clinical experience

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The cost-effectiveness of screening for type 2 diabetes has been estimated. The incremental cost of screening all persons 25 years or older was estimated to be $236,449 per life-year gained and $56,649 per quality adjusted life-year gained. Interestingly, screening was more cost-effective at ages younger than the 45 years currently recommended.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

An external panel of experts reviewed a draft of the guidelines, which were modified in response to the reviewers´ suggestions. A revised draft was posted on the Internet and was presented at the American Association for Clinical Chemistry (AACC) Annual Meeting in July 2000. The recommendations were modified again

in response to oral and written comments and were then reviewed by the Professional Practice Committee of the American Diabetes Association.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Each recommendation is rated based on the quality of scientific evidence. Definitions of the grades of the recommendation (A, B, C, E) are presented at the end of the Major Recommendations field.

Glucose

Use

Diagnosis/Screening

Glucose should be measured in plasma in an accredited laboratory to establish the diagnosis of diabetes. Level of evidence: A

Glucose should be measured in plasma in an accredited laboratory for screening of high-risk individuals. Level of evidence: E

Analysis in an accredited laboratory is not necessary for routine monitoring. Level of evidence: E

Monitoring/Prognosis

Although there is evidence linking high plasma glucose concentrations to adverse outcome, substantially more data are available that directly correlate increased glycated hemoglobin (GHb) with complications of diabetes. Routine measurement of plasma glucose concentrations in an accredited laboratory is not recommended as the primary means of monitoring or evaluating therapy in individuals with diabetes. Level of evidence: E

Analytical Considerations

Preanalytical

Blood for fasting plasma glucose (FPG) analysis should be drawn after the individual has fasted overnight (at least 8 h). Plasma should be separated from the cells within 60 min; if this is not possible, a tube containing a glycolytic inhibitor such as sodium fluoride should be used for collecting the sample. Level of evidence: B

Analytical

Enzymatic methods for glucose analysis are relatively well standardized. Despite the low imprecision at the diagnostic decision limits of 7.0 mmol/L (126 mg/dL) and 11.1 mmol/L (200 mg/dL), classification errors may occur. Because of the

relatively large intraindividual biological variability (coefficients of variation [CVs] of ~5-7%), FPG values of 5.8-6.9 mmol/L (105-125 mg/dL) should be repeated and individuals with FPG of 5.3-5.7 mmol/L (96-104 mg/dL) should be considered for follow-up at intervals shorter than the current American Diabetes Association (ADA) recommendation of every 3 years. Level of evidence: E

Meters

Use

Diagnosis/Screening

There are no published data to support a role for portable meters in the diagnosis of diabetes or for population screening. The imprecision of the meters, coupled with the substantial differences among meters, precludes their use in the diagnosis of diabetes and limits their usefulness in screening for diabetes. Level of evidence: E

Monitoring/Prognosis

Self-monitoring of blood glucose (SMBG) is recommended for all insulin-treated patients with diabetes. For type 1 patients, SMBG is recommended three or more times a day. SMBG may be desirable in patients treated with sulfonylureas or other insulin secretagogues and in all patients not achieving goals. Level of evidence: B

In patients with type 2 diabetes, SMBG may help achieve better control, particularly when therapy is initiated or changed. However, there are no data to support this concept. The role of SMBG in patients with stable type 2 diabetes controlled by diet alone is not known. Level of evidence: C

Analytical Considerations

Preanalytical

Patients should be instructed in the correct use of glucose meters, including quality control. Comparison between SMBG and concurrent laboratory glucose analysis should be performed at regular intervals to evaluate the accuracy of patient results. Level of evidence: B

Analytical

Multiple performance goals for portable glucose meters have been proposed. These targets vary widely and are highly controversial. No published study has achieved the goals proposed by the American Diabetes Association (ADA). Manufacturers should work to improve the imprecision of current meters. Level of evidence: E

We recommend meters that measure and report plasma glucose concentrations to facilitate comparison with assays performed in accredited laboratories. Level of evidence: E

Clinical studies are needed to determine the analytical goals for glucose meters. At a minimum, the end-points should be glycated hemoglobin (GHb) and frequency of hypoglycemic episodes. Ideally, outcomes (e.g., long-term complications and hypoglycemia) should also be examined. Level of evidence: E

Oral Glucose Tolerance Test (OGTT)

The oral glucose tolerance test (OGTT) is not recommended for the routine diagnosis of type 1 or 2 diabetes mellitus. It is recommended for establishing the diagnosis of gestational diabetes mellitus (GDM). Level of evidence: B

Urinary Glucose

Semiquantitative urine glucose testing is not recommended for routine care of patients with diabetes mellitus. Level of evidence: C

Noninvasive or Minimally Invasive Glucose Analyses

Noninvasive glucose analyses cannot be recommended as replacements for SMBG or glucose measurements by an accredited laboratory. Ongoing developments in the field, such as use of the new Gluco Watch Biographer, may influence this recommendation. Level of evidence: E

Ketones

Use

Ketones should be measured in urine or blood by patients with diabetes in the home setting and in the clinic/hospital setting as an adjunct to the diagnosis of diabetic ketoacidosis (DKA). Level of evidence: E

Interpretation

Urine Ketone Determinations

Urine ketone determinations should not be used to diagnose or monitor the course of DKA. Level of evidence: A

Blood Ketone Determinations

Blood ketone determinations that rely on the nitroprusside reaction should be used only as an adjunct to diagnose DKA and should not be used to monitor treatment of DKA. Specific measurement of beta-hydroxybutyric acid (betaHBA) in blood can be used for diagnosis and monitoring of DKA. Further studies are needed to determine whether the test offers any clinical advantage over more traditional management approaches (e.g., measurements of serum CO_2, anion gap, or pH). Level of evidence: E

Glycated Hemoglobin (GHb)

Use

GHb should be measured routinely in all patients with diabetes mellitus to document their degree of glycemic control. Treatment goals should be based on the results of prospective randomized clinical trials such as the Diabetes Control and Complications Trial (DCCT) and United Kingdom Prospective Diabetes Study (UKPDS). These trials have documented the relationship between glycemic control, as quantified by serial determinations of GHb, and risks for the development and progression of chronic complications of diabetes.

Laboratories should be aware of potential interferences, including hemoglobinopathies, that may affect GHb test results. In selecting assay methods, laboratories should consider the potential for interferences in their particular patient population. Level of evidence: A

Analytical Considerations

Laboratories should use only GHb assay methods that are certified by the National Glycohemoglobin Standardization Program (NGSP) as traceable to the DCCT reference. In addition, laboratories that measure GHb should participate in a proficiency-testing program, such as the College of American Pathologists (CAP) Glycohemoglobin Survey, that uses fresh blood samples with targets set by the National Glycohemoglobin Standardization Program (NGSP) Laboratory Network. Level of evidence: B

Analytical

Laboratories should use GHb assay methods with an interassay coefficient of variation (CV) <5% (ideally <3%). At least two control materials with different mean values should be analyzed as an independent measure of assay performance. Laboratories should verify specimens below the lower limit of the reference interval or >15% by repeat testing. If Schiff base (labile pre-Hb A_{1c}) interferes with the assay method, it should be removed before assay. Level of evidence: C

Interpretation

Clinical Application

Treatment goals should be based on ADA recommendations, which include maintaining GHb concentrations <7% and reevaluation of the treatment regimen for GHb values >8%. (Note that these values are applicable only if the assay method is certified as traceable to the DCCT reference.) GHb testing should be performed at least biannually in all patients and quarterly for patients whose therapy has changed or who are not meeting treatment goals. Level of evidence: B

Genetic Markers

Use

Diagnosis/Screening

Type 1 Diabetes

Routine measurement of genetic markers is not of value at this time for the diagnosis or management of patients with type 1 diabetes. For selected diabetic syndromes, valuable information can be obtained with definition of diabetes-associated mutations. Level of evidence: E

Type 2 Diabetes and Maturity Onset Diabetes of Youth (MODY)

There is no role for routine genetic testing in patients with type 2 diabetes. These studies should be confined to the research setting and evaluation of specific syndromes. Level of evidence: E

Autoimmune Markers

Use

Islet cell autoantibodies are recommended for screening of nondiabetic family members who wish to donate part of their pancreas for transplantation to a relative with end stage, immune-mediated (type 1) diabetes. Islet cell autoantibodies are not recommended for routine diagnosis of diabetes or for screening. Level of evidence: E

Diagnosis/Screening

Screening

Screening of relatives of patients with type 1 diabetes or of persons in the general population for islet cell autoantibodies is not recommended at present. Level of evidence: E

Monitoring/Prognosis

There is currently no role for measurement of islet cell autoantibodies in the monitoring of patients in clinical practice. Islet cell autoantibodies are measured in research protocols and some clinical trials as surrogate end-points. Level of evidence: E

Analytical Considerations

It is important that autoantibodies be measured only in an accredited laboratory with an established quality-control program and participation in a proficiency-testing program. Level of evidence: E

Microalbuminuria

Annual microalbumin testing of patients without clinical proteinuria should begin in pubertal or postpubertal individuals 5 years after diagnosis of type 1 diabetes

and at the time of diagnosis of type 2 diabetes. The role of testing is unclear in patients under treatment with angiotensin-converting enzyme inhibitors and in those with a short life expectancy. Level of evidence: E

Analytical Considerations

Analytical

The analytical CV of methods to measure microalbuminuria should be <15%. Level of evidence: E

Premeasurement

Acceptable samples to test for increased urinary albumin excretion are timed (e.g., 12 or 24 h) collections for measurement of albumin concentration and timed or untimed samples for measurement of the albumin:creatinine ratio. For screening, an untimed sample for albumin measurement (without creatinine) may be considered if a concentration cutoff is used that allows high sensitivity for detection of an increased albumin excretion rate. Level of evidence: E

Measurement: Detection Limit, Imprecision

Semiquantitative or qualitative screening tests for microalbuminuria should be positive in >95% of patients with microalbuminuria to be useful for screening. Positive results must be confirmed by analysis in an accredited laboratory. Level of evidence: E

Miscellaneous Potentially Important Analytes

Insulin and Precursors

There is no role for routine testing for insulin, C-peptide, or proinsulin in most patients with diabetes. Differentiation between type 1 and type 2 diabetes may, in most cases, be made based on the clinical presentation and subsequent course. There is no role for measurement of insulin concentration in the diagnosis of the metabolic syndrome because knowledge of this value does not alter the management of these patients.

These assays are useful primarily for research purposes and, in rare cases, to identify patients with an absolute requirement for insulin before switching to oral agents, or to assist patients in obtaining insurance coverage for continuous subcutaneous infusion pumps.

A possible role for measurement of fasting insulin or the assessment of insulin resistance is in the evaluation of patients with polycystic ovary syndrome who may be candidates for treatment aimed at lowering insulin resistance in the absence of overt diabetes or glucose intolerance. Level of evidence: E

Insulin Antibodies

There is no published evidence to support the use of insulin antibody testing for routine care of patients with diabetes. Level of evidence: E

Amylin

Assays for amylin are not clinically useful in the management of diabetes. These studies should be confined to the research setting. Level of evidence: E

Leptin

Routine measurement of plasma leptin concentrations is not of value at this time for the evaluation or management of patients with diabetes or obesity. Level of evidence: E

Lipids

All adults with diabetes should receive annual lipid profiles. Individuals at low risk, i.e., those with low-density lipids (LDL) <2.6 mmol/L (100 mg/dL) and high-density lipids (HDL) >1.15 mmol/L (45 mg/dL) for men and >1.4 mmol/L (55 mg/dL) for women, may be screened less frequently. Because many patients with diabetes are candidates for lipid-lowering therapy, more frequent measurements may be required until control is achieved. Level of evidence: A

Emerging Considerations: New Cardiovascular Risk Factors

Measurement of nontraditional cardiovascular risk factors, such as C-reactive protein, fibrinogen, apolipoprotein (apo) B, and homocysteine, is not recommended for routine assessment of risk in patients with diabetes because the results would not lead to changes of therapy. Should ongoing trials support the use of folic acid to lower coronary artery disease (CAD) by lowering homocysteine concentrations, or the use of other specific therapies aimed at one or more nontraditional risk factors, this recommendation may change. Level of evidence: E

Definitions:

A

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C

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- Evidence from case series or case reports

Conflicting evidence with the weight of evidence supporting the recommendation

E

Expert consensus or clinical experience

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate laboratory analysis in the diagnosis and management of diabetes mellitus

POTENTIAL HARMS

Not stated

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Sacks DB, Bruns DE, Goldstein DE, Maclaren NK, McDonald JM, Parrott M. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Clin Chem 2002 Mar;48(3):436-72. [267 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002

GUIDELINE DEVELOPER(S)

National Academy of Clinical Biochemistry - Professional Association

SOURCE(S) OF FUNDING

National Academy of Clinical Biochemistry

GUIDELINE COMMITTEE

National Academy of Clinical Biochemistry Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the National Academy of Clinical Biochemistry (NACB) Web site:

- Word Format
- Portable Document Format (PDF)

Print copies: National Academy of Clinical Biochemistry publications are available through American Association for Clinical Chemistry (AACC) Press. To make a purchase or request a catalog, contact AACC Customer Service at 202-857-0717 or custserv@aacc.org.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on April 10, 2003. The information was verified by the guideline developer on June 5, 2003.

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